

Food and Drug Administration Silver Spring, MD 20993

Steven A. Kates, Ph.D. Vice President Citius Pharmaceuticals, LLC 63 Great Road Maynard, MA 01754

RE: NDA 202088

Suprenza™ (phentermine hydrochloride) orally disintegrating tablet, CIV MA #25

Dear Dr. Kates:

This letter notifies Citius Pharmaceuticals, LLC (Citius) and, by copy, Akrimax Pharmaceuticals, LLC (Akrimax), agent for Suprenza™ (phentermine hydrochloride) orally disintegrating tablet CIV (Suprenza), that as part of its routine monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed the homepage (webpage) of a website for Suprenza.¹ This webpage is false or misleading because it omits risk information, includes unsubstantiated efficacy claims for Suprenza, and omits material facts. Thus, the webpage misbrands Suprenza within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). See 21 CFR 202.1(e)(5)(i), (iii); (e)(6)(i).

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Suprenza.²

According to the INDICATIONS AND USAGE section of the FDA-approved product labeling (PI) (in pertinent part):

Suprenza is indicated as a short-term (a few weeks) adjunct in a regimen of weight reduction based on exercise, behavioral modification and caloric restriction in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30 kg/m², or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia).

. . .

¹ Suprenza homepage at http://www.leanonsuprenza.com (last accessed June 9, 2014)

² This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

The limited usefulness of agents of this class, including Suprenza, should be measured against possible risk factors inherent in their use. . .

Suprenza is contraindicated in patients with a history of cardiovascular disease; during or within 14 days following the administration of monoamine oxidase inhibitors; in patients with hyperthyroidism, glaucoma, agitated states, or history of drug abuse; in pregnant or nursing patients; and in patients with a known hypersensitivity, or idiosyncrasy to the sympathomimetic amines. The PI for Suprenza includes Warnings and Precautions regarding coadministration with other drug products for weight loss, primary pulmonary hypertension, valvular heart disease, development of tolerance and discontinuation, effect on the ability to engage in potentially hazardous tasks, risk of abuse and dependence, usage with alcohol, use in patients with hypertension, use in patients on insulin or oral hypoglycemic medications for diabetes mellitus, and risk of allergic reactions due to tartrazine. Adverse events have been reported in the cardiovascular, central nervous, gastrointestinal, allergic, and endocrine systems.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to the consequences that may result from the use of the drug as recommended or suggested by the materials.

The webpage includes numerous efficacy claims and presentations for Suprenza; however, it omits **all** of the contraindications and adverse reactions associated with its use. Furthermore, while the webpage does contain information regarding the risk of co-administration of Suprenza with other drug products for weight loss, it fails to disclose any of the other warnings and precautions associated with the drug. By omitting serious and frequently occurring risks associated with Suprenza, the webpage misleadingly suggests that Suprenza is safer than has been demonstrated. We note that the statement "Click here for full Prescribing Information" (emphasis original) is included on the webpage. However, this does not mitigate the misleading omission of risk information.

Unsubstantiated Efficacy Claims

Promotional materials are misleading if they contain a representation or suggestion that a drug is more effective than has been demonstrated by substantial evidence or substantial clinical experience.

The webpage includes an image of a woman squeezing together lettered blocks that spell the word "LEAN." The webpage also includes the following claims (emphasis original):

- "Stay on course for success with The Suprenza LEAN Program"
- "It's time to take control. . .and get LEAN"
- "www.leanonsuprenza.com"

The totality of these claims and presentations misleadingly suggests that patients will become "LEAN" as a result of therapy with Suprenza. However, FDA is not aware of substantial evidence or substantial clinical experience to support this implication. The term "LEAN" is an amorphous cosmetic descriptor, commonly understood to mean thin, slim, or slender, that was not associated with any clinical endpoints in the studies for phentermine. The CLINICAL STUDIES section of the PI describes the efficacy of phentermine as the following (in pertinent part):

In relatively short-term clinical trials, adult obese subjects instructed in dietary management and treated with "anorectic" drugs lost more weight on the average than those treated with placebo and diet.

The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week.

If you have data to support the claims and presentations cited above, please submit them to FDA for review.

Omission of Material Facts

The webpage makes representations about Suprenza's use for weight loss, but it misleadingly omits material information regarding the FDA-approved indication for the drug. Specifically, the webpage fails to disclose the minimum initial body mass index (BMI) for which treatment with Suprenza is indicated, and the requisite presence of other risk factors in patients with an initial BMI of greater than or equal to 27 kg/m². The INDICATIONS AND USAGE section of the PI states the following (in pertinent part):

Suprenza is indicated as a short-term (a few weeks) adjunct in a regimen of weight reduction based on exercise, behavioral modification and caloric restriction in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30 kg/m², or greater than or equal to 27 kg/m² in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia).

Conclusion and Requested Action

For the reasons discussed above, the webpage misbrands Suprenza within the meaning of the FD&C Act, and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). See 21 CFR 202.1(e)(5)(i), (iii); (e)(6)(i).

OPDP requests that Citius immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before June 23, 2014, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Suprenza that contain violations such as those described above, and explaining your plan for discontinuing use of such materials.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Professional Drug Promotion, 5901-B Ammendale Road, Beltsville,

Maryland 20705-1266 or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA #25 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Suprenza comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Ankur Kalola, Pharm.D.
Regulatory Review Officer
Office of Prescription Drug Promotion

{See appended electronic signature page}

Adora Ndu, Pharm.D.
Acting Team Leader
Office of Prescription Drug Promotion

cc: Keith S. Rotenberg, Ph.D.
Corporate Vice President, Chief Scientific Officer
Akrimax Pharmaceuticals, LLC
11 Commerce Dr. Suite 100
Cranford, NJ 07016

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANKUR S KALOLA
06/09/2014

ADORA NDU
06/09/2014